

NMCP COVID-19 Literature Report #63: Friday, 12 March 2021

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Purpose: These weekly reports, published on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

Statistics

Global today: 118,719,900 confirmed cases and 2,632,147 deaths in 192 countries/regions

5 MAR 2021: 115,760,047 confirmed cases and 2,571,789 deaths in 192 countries/regions

26 FEB 2021: 113,111,157 confirmed cases and 2,510,125 deaths in 192 countries/regions

19 FEB 2021: 110,439,431 confirmed cases and 2,444,329 deaths in 192 countries/regions

United States*

top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	29,287,115	3,614,852	2,716,112	1,962,651	1,720,199	1,204,323
Deaths	530,833	55,160	46,007	32,040	48,690	23,123

*see [census.gov](https://www.census.gov) for current US Population data; NA: not all data available

[JHU CSSE](https://csse.jhu.edu/) as of 1000 EDT 12 March 2021

Virginia is ranked 17th in cases and 17th in deaths.

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	592,214	18,739	8,923	11,918	15,340	7,946	7,082	31,630
Hospitalizations	25,216	869	307	322	844	603	406	1,341
Deaths	9,961	252	140	199	225	154	173	348

[VA DOH](https://www.vadepa.org) as of 1000 EDT 12 March 2021

One Year Later

11 March 2020: "There are now more than 118,000 cases in 114 countries, and 4,291 people have lost their lives" ([WHO](#)).

There are numerous retrospective articles about the pandemic anniversary. Here are a few examples:

- "March 11, 2020: The day everything changed" ([NPR](#)).
- "A pandemic year" ([WashPo](#)).
- "'Then the world caved in': 9 experts describe the day they realized Covid-19 was here to stay" ([STAT](#)).
- "How the US pandemic response went wrong—and what went right—during a year of COVID" ([SciAm](#)).
- "Tom Hanks, the NBA, and COVID's day of reckoning in the US: An oral history" ([BuzzFeed](#)).

Calls and Webinars

TOPIC: Equity in Vaccination: A Plan to Work with Communities of Color Toward COVID-19 Recovery and Beyond

"As the COVID-19 vaccination campaign unfolds, it is critical that vaccines are delivered fairly and equitably—so that everyone has access. Just as pressing is the need to address the pandemic's disproportionate adverse effects on Black, Indigenous, and People of Color (BIPOC) communities across the United States.

As a result of longstanding disparities, the number of cases, hospitalizations, and deaths related to COVID-19 are significantly higher in BIPOC communities, and members of these groups are among those hit the hardest by the pandemic's economic and social upheavals.

A new plan released by CommuniVax, Equity in Vaccination: A Plan to Work with Communities of Color Toward COVID-19 Recovery and Beyond, provides elected and appointed officials with the tools to create, implement, and support a vaccination campaign that works with BIPOC communities to remedy COVID-19 impacts, prevent even more health burdens, lay the foundation for unbiased healthcare delivery, and enable broader social change and durable community-level opportunities.

Hosted by CommuniVax and the Johns Hopkins Center for Health Security, this webinar will discuss the specific recommendations made in the report and share experiences from local initiatives, so officials can consider adopting them as they

implement COVID-19 vaccination campaigns in their own towns, cities, and states."

WHEN: 18 March 2021 1400–1500 ET

REGISTER: https://jh.zoom.us/webinar/register/WN_oTIScqBaTeCfrd0IBUCkcA

Special Reports

CDC: [Updated Healthcare Infection Prevention and Control Recommendations in Response to COVID-19 Vaccination](#) (updated 10 March 2021)

Updates to visitation to post-acute care facilities, including nursing homes, and work restriction for asymptomatic healthcare personnel. See website for full outline of guidance.

CDC: [Interim Public Health Recommendations for Fully Vaccinated People](#) (updated 08 March 2021)

"This is the first set of public health recommendations for fully vaccinated people. This guidance will be updated and expanded based on the level of community spread of SARS-CoV-2, the proportion of the population that is fully vaccinated, and the rapidly evolving science on COVID-19 vaccines.

For the purposes of this guidance, people are considered fully vaccinated for COVID-19 ≥2 weeks after they have received the second dose in a 2-dose series (Pfizer-BioNTech or Moderna), or ≥2 weeks after they have received a single-dose vaccine (Johnson and Johnson (J&J)/Janssen).

The following recommendations apply to non-healthcare settings.

Fully vaccinated people can:

- Visit with other fully vaccinated people indoors without wearing masks or physical distancing
- Visit with unvaccinated people from a single household who are at low risk for severe COVID-19 disease indoors without wearing masks or physical distancing
- Refrain from quarantine and testing following a known exposure if asymptomatic

For now, fully vaccinated people should continue to:

- Take precautions in public like wearing a well-fitted mask and physical distancing
- Wear masks, practice physical distancing, and adhere to other prevention measures when visiting with unvaccinated people who are at increased risk for severe COVID-19

disease or who have an unvaccinated household member who is at increased risk for severe COVID-19 disease

- Wear masks, maintain physical distance, and practice other prevention measures when visiting with unvaccinated people from multiple households
- Avoid medium- and large-sized in-person gatherings
- Get tested if experiencing COVID-19 symptoms
- Follow guidance issued by individual employers
- Follow CDC and health department travel requirements and recommendations"

NIH: [The COVID-19 Treatment Guidelines Panel's Statement on the Use of Tocilizumab for the Treatment of COVID-19](#) (05 March 2021)

"Based on the collective evidence from the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) and Randomized Evaluation of COVID-19 Therapy (RECOVERY) trials, the COVID-19 Treatment Guidelines Panel (the Panel) has determined the following:

- The Panel recommends the use of tocilizumab^a (single intravenous dose of 8 mg/kg of actual body weight, up to 800 mg) in combination with dexamethasone (6 mg daily for up to 10 days)^b in certain hospitalized patients who are exhibiting rapid respiratory decompensation due to COVID-19.^c The patients included in this population are:
 - Recently hospitalized patients^d who have been admitted to the intensive care unit (ICU) within the prior 24 hours and who require invasive mechanical ventilation, noninvasive mechanical ventilation (NIV), or high-flow nasal canula (HFNC) oxygen (>0.4 FiO₂/30 L/min of oxygen flow) (BIIa); or
 - Recently hospitalized patients^d (not in the ICU) with rapidly increasing oxygen needs who require NIV or HFNC and have significantly increased markers of inflammation (BIIa) (Note: The RECOVERY trial inclusion criterion for inflammation was C-reactive protein [CRP] ≥75 mg/L; see details below).
- For hospitalized patients with hypoxemia who require conventional oxygen supplementation, the Panel recommends using one of the following options: remdesivir (BIIa), dexamethasone plus remdesivir (BIII), or dexamethasone alone (BI) (see Therapeutic Management of Adults With COVID-19).
 - There is insufficient evidence to specify which of these patients would benefit from the addition of tocilizumab. Some Panel members would also give tocilizumab to patients who are exhibiting rapidly increasing oxygen needs while on dexamethasone and have a CRP ≥75 mg/L but who do not yet require NIV or HFNC, as described above.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

^a Use of tocilizumab should be avoided in patients with any of the following: (1) significant immunosuppression, particularly in those with a history of recent use of other biologic immunomodulating drugs; (2) alanine transaminase >5 times the upper limit of normal; (3) high risk for gastrointestinal perforation; (4) an uncontrolled, serious bacterial, fungal, or non-SARS-CoV-2 viral infection; (5) absolute neutrophil count <500 cells/ μ L; or (6) platelet count <50,000 cells/ μ L.

^b As an alternative to dexamethasone, corticosteroids at a dose equivalent to dexamethasone 6 mg are acceptable (see Corticosteroids).

^c Respiratory decompensation should be due to progressive COVID-19 and not due to alternative causes, such as volume overload or asthma exacerbation.

^d For example, within 3 days. Median days of hospitalization until randomization was 1.2 days (IQR 0.8–2.8 days) in REMAP-CAP and 2 days (IQR 1–5 days) in the RECOVERY trial.¹⁰

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

11 March 2021

Clin Infect Dis: [Transmission of SARS-CoV-2 from asymptomatic and presymptomatic individuals in healthcare settings despite medical masks and eye protection](#)

"We describe 3 instances of SARS-CoV-2 transmission despite medical masks and eye protection, including transmission despite the source person being masked, transmission despite the exposed person being masked, and transmission despite both parties being masked. Whole genome sequencing confirmed perfect homology between source and exposed persons' viruses in all cases."

JAMA: [Immunogenicity of the Ad26.COV2.S Vaccine for COVID-19](#)

"Question: Is the Ad26.COV2.S vaccine immunogenic in humans, how quickly does it raise antibody responses, and what types of immune responses are elicited?

Findings: This randomized, double-blind, placebo-controlled phase 1 clinical trial of Ad26.COV2.S enrolled 25 participants. Antibodies were detected in vaccine recipients by

day 8 and were observed in all vaccine recipients by day 57 after a single immunization. T-cell responses were also generated in vaccine recipients.

Meaning: In this phase 1 study, a single immunization with Ad26.COV2.S induced rapid binding and neutralization antibody responses as well as cellular immune responses."

JAMA Netw Open: [Experiences of Latinx Individuals Hospitalized for COVID-19: A Qualitative Study](#)

"Question: Can experiences of Latinx adults hospitalized with coronavirus disease 2019 (COVID-19) inform improvements to public health and health care?

Findings: In this qualitative study of 60 Latinx adults, participants reported COVID-19 misinformation, felt COVID-19 compounded existing social disadvantage, and risked infection because of the need to work. Participants hesitated to seek hospital care because of immigration and economic concerns.

Meaning: These findings suggest that to contain community spread and reduce unnecessary morbidity, immigration, employment, and economic distress must be addressed through tailored public health messaging and public policy interventions that improve economic conditions."

10 March 2021

BMJ: [Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study](#)

"Objective To establish whether there is any change in mortality from infection with a new variant of SARS-CoV-2, designated a variant of concern (VOC-202012/1) in December 2020, compared with circulating SARS-CoV-2 variants.

Design Matched cohort study.

Setting Community based (pillar 2) covid-19 testing centres in the UK using the TaqPath assay (a proxy measure of VOC-202012/1 infection).

Participants 54 906 matched pairs of participants who tested positive for SARS-CoV-2 in pillar 2 between 1 October 2020 and 29 January 2021, followed-up until 12 February 2021. Participants were matched on age, sex, ethnicity, index of multiple deprivation, lower tier local authority region, and sample date of positive specimens, and differed only by detectability of the spike protein gene using the TaqPath assay.

Main outcome measure Death within 28 days of the first positive SARS-CoV-2 test result.

Results The mortality hazard ratio associated with infection with VOC-202012/1 compared with infection with previously circulating variants was 1.64 (95% confidence interval 1.32 to 2.04) in patients who tested positive for covid-19 in the community. In this comparatively low risk group, this represents an increase in deaths from 2.5 to 4.1 per 1000 detected cases.

Conclusions The probability that the risk of mortality is increased by infection with VOC-202012/01 is high. If this finding is generalisable to other populations, infection with VOC-202012/1 has the potential to cause substantial additional mortality compared with previously circulating variants. Healthcare capacity planning and national and international control policies are all impacted by this finding, with increased mortality lending weight to the argument that further coordinated and stringent measures are justified to reduce deaths from SARS-CoV-2."

Clin Infect Dis: [Effectiveness of three versus six feet of physical distancing for controlling spread of COVID-19 among primary and secondary students and staff: A retrospective, state-wide cohort study](#)

"National and international guidelines differ about the optimal physical distancing between students for prevention of SARS-CoV-2 transmission; studies directly comparing the impact of ≥ 3 versus ≥ 6 feet of physical distancing policies in school settings are lacking. Thus, our objective was to compare incident cases of SARS-CoV-2 in students and staff in Massachusetts public schools among districts with different physical distancing requirements. State guidance mandates masking for all school staff and for students in grades 2 and higher; the majority of districts required universal masking."

Clin Infect Dis: [Impact of the COVID-19 Vaccine on Asymptomatic Infection Among Patients Undergoing Pre-Procedural COVID-19 Molecular Screening](#)

"We conducted a retrospective cohort study of consecutive, asymptomatic adult patients ($n = 39,156$) within a large United States healthcare system who underwent 48,333 pre-procedural SARS-CoV-2 molecular screening tests between December 17, 2020 and February 8, 2021. The primary exposure of interest was vaccination with at least one dose of an mRNA COVID-19 vaccine. The primary outcome was relative risk of a positive SARS-CoV-2 molecular test among those asymptomatic persons who had received at least one dose of vaccine, as compared to persons who had not received vaccine during the same time period. Relative risk was adjusted for age, sex, race/ethnicity, patient residence relative to the hospital (local vs. non-local), healthcare system regions, and repeated screenings among patients using mixed effects log-binomial regression.

Positive molecular tests in asymptomatic individuals were reported in 42 (1.4%) of 3,006 tests performed on vaccinated patients and 1,436 (3.2%) of 45,327 tests performed on unvaccinated patients ($RR=0.44$ 95% CI: 0.33-0.60; $p<.0001$). Compared to unvaccinated

patients, the risk of asymptomatic SARS-CoV-2 infection was lower among those >10 days after 1 st dose (RR=0.21; 95% CI: 0.12-0.37; p<.0001) and >0 days after 2 nd dose (RR=0.20; 95% CI: 0.09-0.44; p<.0001) in the adjusted analysis.

COVID-19 vaccination with an mRNA-based vaccine showed a significant association with a reduced risk of asymptomatic SARS-CoV-2 infection as measured during pre-procedural molecular screening. The results of this study demonstrate the impact of the vaccines on reduction in asymptomatic infections supplementing the randomized trial results on symptomatic patients."

JAMA Netw Open: [Association of Age With Likelihood of Developing Symptoms and Critical Disease Among Close Contacts Exposed to Patients With Confirmed SARS-CoV-2 Infection in Italy](#)

"Question: What is the association of age with the likelihood of developing respiratory symptoms or fever greater than or equal to 37.5 °C and the association of age with the likelihood of progressing to critical disease after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection?

Findings: In this cohort study, 5484 quarantined case contacts were monitored daily for symptoms for at least 2 weeks and were tested for infection via real-time reverse transcriptase–polymerase chain reaction or serological screening more than 1 month after identification. Only 26.1% of infected individuals younger than 60 years developed respiratory symptoms or fever greater than or equal to 37.5 °C, but 6.6% of infected participants aged 60 years or older developed critical disease.

Meaning: The low proportion of children and young adults who developed symptoms highlights the possible challenges in readily identifying SARS-CoV-2 infections."

JAMA Netw Open: [Risk Factors Associated With SARS-CoV-2 Seropositivity Among US Health Care Personnel](#)

"Question: What risk factors are associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seropositivity among health care personnel (HCP) inside and outside the workplace?

Findings: In this cross-sectional study of 24 749 HCP in 3 US states, contact with an individual with known coronavirus disease 2019 (COVID-19) exposure outside the workplace was the strongest risk factor associated with SARS-CoV-2 seropositivity, along with living in a zip code with higher COVID-19 incidence. None of the assessed workplace factors were associated with seropositivity.

Meaning: In this study, most risk factors associated with SARS-CoV-2 infection among HCP were outside the workplace, suggesting that current infection prevention strategies in health care are effective in preventing patient-to-HCP transmission in the workplace."

MMWR: [Racial and Ethnic Disparities in COVID-19 Incidence by Age, Sex, and Period Among Persons Aged <25 Years — 16 U.S. Jurisdictions, January 1–December 31, 2020](#)

"What is already known about this topic? U.S. racial and ethnic minority groups have been disproportionately affected by COVID-19.

What is added by this report? Racial and ethnic disparities in COVID-19 incidence among persons aged <25 years in 16 U.S. jurisdictions evolved during the pandemic. Disparities were substantial during January–April and generally decreased during May–December, largely because of a greater increase in incidence among White persons, rather than a decline among racial and ethnic minority groups. The largest persistent disparities involved Native Hawaiian and Pacific Islander, American Indian or Alaska Native, and Hispanic persons.

What are the implications for public health practice? Ensuring equitable and timely access to preventive measures, including testing, safe work and education settings, and vaccination when eligible is important to address racial/ethnic disparities."

Nat Med: [Attributes and predictors of long COVID](#)

"Reports of long-lasting coronavirus disease 2019 (COVID-19) symptoms, the so-called 'long COVID', are rising but little is known about prevalence, risk factors or whether it is possible to predict a protracted course early in the disease. We analyzed data from 4,182 incident cases of COVID-19 in which individuals self-reported their symptoms prospectively in the COVID Symptom Study app¹. A total of 558 (13.3%) participants reported symptoms lasting ≥28 days, 189 (4.5%) for ≥8 weeks and 95 (2.3%) for ≥12 weeks. Long COVID was characterized by symptoms of fatigue, headache, dyspnea and anosmia and was more likely with increasing age and body mass index and female sex. Experiencing more than five symptoms during the first week of illness was associated with long COVID (odds ratio = 3.53 (2.76–4.50)). A simple model to distinguish between short COVID and long COVID at 7 days (total sample size, n = 2,149) showed an area under the curve of the receiver operating characteristic curve of 76%, with replication in an independent sample of 2,472 individuals who were positive for severe acute respiratory syndrome coronavirus 2. This model could be used to identify individuals at risk of long COVID for trials of prevention or treatment and to plan education and rehabilitation services."

NEJM: [Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine](#)

"We found that a single dose of mRNA vaccine elicited rapid immune responses in seropositive participants, with postvaccination antibody titers that were similar to or exceeded titers found in seronegative participants who received two vaccinations. Whether a single dose of mRNA vaccine provides effective protection in seropositive persons requires investigation."

09 March 2021

Clin Infect Dis: [COVID-19 Associated Pulmonary Aspergillosis in Mechanically Ventilated Patients](#)

"COVID-19 associated pulmonary aspergillosis (CAPA) occurs in critically ill COVID-19 patients. Risks and outcomes remain poorly understood.

A retrospective cohort study of adult mechanically ventilated COVID-19 patients admitted to five Johns Hopkins hospitals was conducted between March and August 2020. CAPA was defined using composite clinical criteria. Fine and Gray competing risks regression was used to analyze clinical outcomes and multilevel mixed-effects ordinal logistic regression was used to compare longitudinal disease severity scores.

Amongst the cohort of 396 people, 39 met criteria for CAPA. Compared to those without, patients with CAPA were more likely to have underlying pulmonary vascular disease (41% vs 21.6%, p=0.01), liver disease (35.9% vs 18.2%, p=0.02), coagulopathy (51.3% vs 33.1%, p=0.03), solid tumors (25.6% vs 10.9%, p=0.017), multiple myeloma (5.1% vs 0.3%, p=0.027), corticosteroid exposure during index admission (66.7% vs 42.6%, p=0.005), and had a lower BMI (median 26.6 vs 29.9, p=0.04). People with CAPA had worse outcomes as measured by ordinal severity of disease scores, requiring longer time to improvement (adjusted odds ratio 1.081.091.1, p<0.001), and advancing in severity almost twice as fast (subhazard ratio, sHR 1.31.82.5, p<0.001). People with CAPA were intubated twice as long as those without (sHR) 0.40.50.6, p<0.001) and had a longer hospital length of stay [median (IQR) 41.1 (20.5, 72.4) vs 18.5 (10.7, 31.8), p<0.001].

CAPA is associated with poor outcomes. Attention towards preventative measures (screening and/or prophylaxis) is warranted in people with high risk of developing CAPA."

J Infect Dis: [Prevention of COVID-19 among older adults receiving pneumococcal conjugate vaccine suggests interactions between Streptococcus pneumoniae and SARS-CoV-2 in the respiratory tract](#)

"While secondary pneumococcal pneumonia occurs less commonly after COVID-19 than after other viral infections, it remains unclear whether other interactions occur between SARS-CoV-2 and *Streptococcus pneumoniae*.

We probed potential interactions between these pathogens among adults aged ≥65y by measuring associations of COVID-19 outcomes with pneumococcal vaccination (13-valent conjugate and 23-valent polysaccharide; PCV13, PPSV23). We estimated adjusted hazard ratios (aHRs) using Cox proportional hazards models with doubly-robust inverse-propensity weighting. We assessed effect modification by antibiotic exposure to further test the biologic plausibility of a causal role for pneumococci.

Among 531,033 adults, there were 3,677 COVID-19 diagnoses, leading to 1,075 hospitalizations and 334 fatalities, between 1 March-22 July, 2020. Estimated aHRs for COVID-19 diagnosis, hospitalization, and mortality associated with prior PCV13 receipt were 0.65 (95% confidence interval: 0.59-0.72), 0.68 (0.57-0.83), and 0.68 (0.49-0.95), respectively. Prior PPSV23 receipt was not associated with protection against the three outcomes. COVID-19 diagnosis was not associated with prior PCV13 within 90 days following antibiotic receipt, whereas aHR estimates were 0.65 (0.50-0.84) and 0.62 (0.56-0.70) during risk periods 91-365d and >365d following antibiotic receipt, respectively.

Reduced risk of COVID-19 among PCV13 recipients, transiently attenuated by antibiotic exposure, suggests pneumococci may interact with SARS-CoV-2."

Lancet Child Adolesc Health: [Factors linked to severe outcomes in multisystem inflammatory syndrome in children \(MIS-C\) in the USA: a retrospective surveillance study](#)

"Multisystem inflammatory syndrome in children (MIS-C) is a newly identified and serious health condition associated with SARS-CoV-2 infection. Clinical manifestations vary widely among patients with MIS-C, and the aim of this study was to investigate factors associated with severe outcomes.

In this retrospective surveillance study, patients who met the US Centers for Disease Control and Prevention (CDC) case definition for MIS-C (younger than 21 years, fever, laboratory evidence of inflammation, admitted to hospital, multisystem [≥2] organ involvement [cardiac, renal, respiratory, haematological, gastrointestinal, dermatological, or neurological], no alternative plausible diagnosis, and either laboratory confirmation of SARS-CoV-2 infection by RT-PCR, serology, or antigen test, or known COVID-19 exposure within 4 weeks before symptom onset) were reported from state and local health departments to the CDC using standard case-report forms. Factors assessed for potential

links to severe outcomes included pre-existing patient factors (sex, age, race or ethnicity, obesity, and MIS-C symptom onset date before June 1, 2020) and clinical findings (signs or symptoms and laboratory markers). Logistic regression models, adjusted for all pre-existing factors, were used to estimate odds ratios between potential explanatory factors and the following outcomes: intensive care unit (ICU) admission, shock, decreased cardiac function, myocarditis, and coronary artery abnormalities.

1080 patients met the CDC case definition for MIS-C and had symptom onset between March 11 and Oct 10, 2020. ICU admission was more likely in patients aged 6–12 years (adjusted odds ratio 1·9 [95% CI 1·4–2·6] and patients aged 13–20 years (2·6 [1·8–3·8]), compared with patients aged 0–5 years, and more likely in non-Hispanic Black patients, compared with non-Hispanic White patients (1·6 [1·0–2·4]). ICU admission was more likely for patients with shortness of breath (1·9 [1·2–2·9]), abdominal pain (1·7 [1·2–2·7]), and patients with increased concentrations of C-reactive protein, troponin, ferritin, D-dimer, brain natriuretic peptide (BNP), N-terminal pro B-type BNP, or interleukin-6, or reduced platelet or lymphocyte counts. We found similar associations for decreased cardiac function, shock, and myocarditis. Coronary artery abnormalities were more common in male patients (1·5 [1·1–2·1]) than in female patients and patients with mucocutaneous lesions (2·2 [1·3–3·5]) or conjunctival injection (2·3 [1·4–3·7]).

Identification of important demographic and clinical characteristics could aid in early recognition and prompt management of severe outcomes for patients with MIS-C."

Nature: [Emergence of a SARS-CoV-2 variant of concern with mutations in spike glycoprotein](#)

"Continued uncontrolled transmission of the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) in many parts of the world is creating the conditions for significant virus evolution. Here, we describe a new SARS-CoV-2 lineage (501Y.V2) characterised by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) that may have functional significance. This lineage was identified in South Africa after the first epidemic wave in a severely affected metropolitan area, Nelson Mandela Bay, located on the coast of the Eastern Cape Province. This lineage spread rapidly, becoming dominant in the Eastern Cape, Western Cape and KwaZulu-Natal Provinces within weeks. Whilst the full significance of the mutations is yet to be determined, the genomic data, showing the rapid expansion and displacement of other lineages in multiple regions, suggest that this lineage is associated with a selection advantage, most plausibly as a result of increased transmissibility or immune escape."

08 March 2021

BMJ Health Care Inform: [Performance of national COVID-19 'symptom checkers': a comparative case simulation study](#)

"Identifying those individuals requiring medical care is a basic tenet of the pandemic response. Here, we examine the COVID-19 community triage pathways employed by four nations, specifically comparing the safety and efficacy of national online 'symptom checkers' used within the triage pathway.

A simulation study was conducted on current, nationwide, patient-led symptom checkers from four countries (Singapore, Japan, USA and UK). 52 cases were simulated to approximate typical COVID-19 presentations (mild, moderate, severe and critical) and COVID-19 mimickers (eg, sepsis and bacterial pneumonia). The same simulations were applied to each of the four country's symptom checkers, and the recommendations to refer on for medical care or to stay home were recorded and compared.

The symptom checkers from Singapore and Japan advised onward healthcare contact for the majority of simulations (88% and 77%, respectively). The USA and UK symptom checkers triaged 38% and 44% of cases to healthcare contact, respectively. Both the US and UK symptom checkers consistently failed to identify severe COVID-19, bacterial pneumonia and sepsis, triaging such cases to stay home.

Our results suggest that whilst 'symptom checkers' may be of use to the healthcare COVID-19 response, there is the potential for such patient-led assessment tools to worsen outcomes by delaying appropriate clinical assessment. The key features of the well-performing symptom checkers are discussed."

JAMA: [Acute Allergic Reactions to mRNA COVID-19 Vaccines](#)

"This study examines the incidence of acute allergic reactions to mRNA COVID-19 vaccine administrations in health care employees in Massachusetts."

Lancet Global Health: [Serological evidence of human infection with SARS-CoV-2: a systematic review and meta-analysis](#)

"In this systematic review and meta-analysis, we searched PubMed, Embase, Web of Science, and five preprint servers for articles published in English between Dec 1, 2019, and Dec 22, 2020. Studies evaluating SARS-CoV-2 seroprevalence in humans after the first identified case in the area were included. Studies that only reported serological responses among patients with COVID-19, those using known infection status samples, or any animal experiments were all excluded. All data used for analysis were extracted from included papers. Study quality was assessed using a standardised scale. We estimated age-specific, sex-specific, and race-specific seroprevalence by WHO regions and subpopulations with

different levels of exposures, and the ratio of serology-identified infections to virologically confirmed cases. This study is registered with PROSPERO, CRD42020198253.

16 506 studies were identified in the initial search, 2523 were assessed for eligibility after removal of duplicates and inappropriate titles and abstracts, and 404 serological studies (representing tests in 5 168 360 individuals) were included in the meta-analysis. In the 82 studies of higher quality, close contacts (18·0%, 95% CI 15·7–20·3) and high-risk health-care workers (17·1%, 9·9–24·4) had higher seroprevalence than did low-risk health-care workers (4·2%, 1·5–6·9) and the general population (8·0%, 6·8–9·2). The heterogeneity between included studies was high, with an overall I² of 99·9% ($p<0·0001$). Seroprevalence varied greatly across WHO regions, with the lowest seroprevalence of general populations in the Western Pacific region (1·7%, 95% CI 0·0–5·0). The pooled infection-to-case ratio was similar between the region of the Americas (6·9, 95% CI 2·7–17·3) and the European region (8·4, 6·5–10·7), but higher in India (56·5, 28·5–112·0), the only country in the South-East Asia region with data.

Antibody-mediated herd immunity is far from being reached in most settings. Estimates of the ratio of serologically detected infections per virologically confirmed cases across WHO regions can help provide insights into the true proportion of the population infected from routine confirmation data."

MMWR: [Body Mass Index and Risk for COVID-19–Related Hospitalization, Intensive Care Unit Admission, Invasive Mechanical Ventilation, and Death — United States, March–December 2020](#)

"What is already known about this topic? Obesity increases the risk for severe COVID-19–associated illness.

What is added by this report? Among 148,494 U.S. adults with COVID-19, a nonlinear relationship was found between body mass index (BMI) and COVID-19 severity, with lowest risks at BMIs near the threshold between healthy weight and overweight in most instances, then increasing with higher BMI. Overweight and obesity were risk factors for invasive mechanical ventilation. Obesity was a risk factor for hospitalization and death, particularly among adults aged <65 years.

What are the implications for public health practice? These findings highlight clinical and public health implications of higher BMIs, including the need for intensive management of COVID-19–associated illness, continued vaccine prioritization and masking, and policies to support healthy behaviors."

PNAS: [Higher airborne pollen concentrations correlated with increased SARS-CoV-2 infection rates, as evidenced from 31 countries across the globe](#)

"Pollen exposure weakens the immunity against certain seasonal respiratory viruses by diminishing the antiviral interferon response. Here we investigate whether the same applies to the pandemic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is sensitive to antiviral interferons, if infection waves coincide with high airborne pollen concentrations. Our original hypothesis was that more airborne pollen would lead to increases in infection rates. To examine this, we performed a cross-sectional and longitudinal data analysis on SARS-CoV-2 infection, airborne pollen, and meteorological factors. Our dataset is the most comprehensive, largest possible worldwide from 130 stations, across 31 countries and five continents. To explicitly investigate the effects of social contact, we additionally considered population density of each study area, as well as lockdown effects, in all possible combinations: without any lockdown, with mixed lockdown–no lockdown regime, and under complete lockdown. We found that airborne pollen, sometimes in synergy with humidity and temperature, explained, on average, 44% of the infection rate variability. Infection rates increased after higher pollen concentrations most frequently during the four previous days. Without lockdown, an increase of pollen abundance by 100 pollen/m³ resulted in a 4% average increase of infection rates. Lockdown halved infection rates under similar pollen concentrations. As there can be no preventive measures against airborne pollen exposure, we suggest wide dissemination of pollen–virus coexposure dire effect information to encourage high-risk individuals to wear particle filter masks during high springtime pollen concentrations."

06 March 2021

Clin Infect Dis: [Are some COVID vaccines better than others? Interpreting and comparing estimates of efficacy in trials of COVID-19 vaccines](#)

"COVID-19 vaccine trials provide valuable insight into the safety and efficacy of vaccines, with individually-randomized, placebo-controlled trials being the gold standard in trial design. However, a myriad of variables must be considered as clinical trial data are interpreted and used to guide policy decisions. These variables include factors such as the characteristics of the study population and circulating SARS-CoV-2 strains, the force of infection, the definition and ascertainment of endpoints, the timing of vaccine efficacy assessment, and the potential for performance bias. In this Viewpoint, we discuss critical variables to consider when comparing efficacy measurements across current and future COVID-19 vaccine trials."

05 March 2021

Int J Infect Dis: [Infection sustained by lineage B.1.1.7 of SARS-CoV-2 is characterised by longer persistence and higher viral RNA loads in nasopharyngeal swabs](#)

"Following the announcement on December 2020 about the emergence of a new variant (VOC 202012/01, B.1.1.7 lineage) in the United Kingdom a targeted surveillance was put in place in Abruzzo region (Italy), which allowed to detect 313 persons affected by lineage B.1.1.7, up to the 20th of February 2021. We investigated the results of RT-PCR on nasopharyngeal swabs tested from December 2020 to February 2021, to verify any difference on the viral load and persistence between people infected by lineage B.1.1.7 and others. Statistically significant lower values of CT associated with the detection of the N protein encoding gene (CT N) were observed in persons with lineage B.1.1.7 infection (median CT N = 15.8) in comparison to those infected by other lineages (median CT N = 16.9). A significant longer duration of the persistence of SARS-CoV-2 RNA in nasopharyngeal swabs was observed in persons with lineage B.1.1.7 infection (16 days) in comparison to those infected by other lineages (14 days)."

JAMA Netw Open: [Outcomes and Mortality Among Adults Hospitalized With COVID-19 at US Medical Centers](#)

"This cohort study assesses characteristics and outcomes among adults hospitalized with coronavirus disease 2019 (COVID-19) at US medical centers as well as COVID-19–related mortality over the initial 6 months of the pandemic."

JAMA Neurology: [Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome](#)

"Question: What is the extent of neurologic involvement in US hospitalized children and adolescents with coronavirus disease 2019 (COVID-19)?

Findings: In this study of 1695 patients 21 years or younger hospitalized for acute COVID-19 or multisystem inflammatory syndrome, 365 (22%) had neurologic involvement. Forty-three patients (12%) developed COVID-19–related life-threatening neurologic disorders, 11 (26%) died, and 17 (40%) survived with new neurologic sequelae.

Meaning: In this study, COVID-19–related neurologic involvement was common in hospitalized children and adolescents and mostly transient."

NEJM Catalyst: [The Devastating Impact of Covid-19 on Individuals with Intellectual Disabilities in the United States](#)

"A cross-sectional study of 64,858,460 patients across 547 health care organizations reveals that having an intellectual disability was the strongest independent risk factor for presenting with a Covid-19 diagnosis and the strongest independent risk factor other than

age for Covid-19 mortality. Screening for Covid-19, care coordination, and vaccination efforts should be intense within this population that is less able to consistently use masks and socially distance."

04 March 2021

JAMA Ophthalmol: [SARS-CoV-2 on Ocular Surfaces in a Cohort of Patients With COVID-19 From the Lombardy Region, Italy](#)

"Question: What is the qualitative and quantitative presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the ocular surface in patients with coronavirus disease 2019 (COVID-19) hospitalized in intensive care units at a university hospital in Lombardy, Italy?

Findings: Using reverse transcription–polymerase chain reaction assay, this study found that SARS-CoV-2 was present on the ocular surface in 52 of 91 patients with COVID-19 (57.1%). The virus may also be detected on ocular surfaces in patients with COVID-19 when the nasopharyngeal swab is negative.

Meaning: These results suggest that SARS-CoV-2 may diffuse from ocular surfaces to the body."

Lancet: [Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK \(PRINCIPLE\): a randomised, controlled, open-label, adaptive platform trial](#)

"All three randomised clinical trials that we identified were in hospital settings, and only one assessed azithromycin as a standalone therapy for COVID-19. To our knowledge, PRINCIPLE is the first randomised trial to assess the effectiveness and safety of azithromycin as a standalone treatment for patients with COVID-19 in the community. We found that azithromycin did not substantially improve time to recovery and found little evidence of an effect on admissions to hospital, when used in the community to treat COVID-19.

Taken together, our findings plus the evidence to date suggest that azithromycin is not a sufficiently effective treatment to justify routine use for treatment of COVID-19, neither in the community nor in hospitals."

Nat Med: [Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies](#)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused the global COVID-19 pandemic. Rapidly spreading SARS-CoV-2 variants may jeopardize newly introduced antibody and vaccine countermeasures. Here, using monoclonal antibodies

(mAbs), animal immune sera, human convalescent sera and human sera from recipients of the BNT162b2 mRNA vaccine, we report the impact on antibody neutralization of a panel of authentic SARS-CoV-2 variants including a B.1.1.7 isolate, chimeric strains with South African or Brazilian spike genes and isogenic recombinant viral variants. Many highly neutralizing mAbs engaging the receptor-binding domain or N-terminal domain and most convalescent sera and mRNA vaccine-induced immune sera showed reduced inhibitory activity against viruses containing an E484K spike mutation. As antibodies binding to spike receptor-binding domain and N-terminal domain demonstrate diminished neutralization potency in vitro against some emerging variants, updated mAb cocktails targeting highly conserved regions, enhancement of mAb potency or adjustments to the spike sequences of vaccines may be needed to prevent loss of protection in vivo."

Pediatr Blood Cancer: [Children and young adults hospitalized for severe COVID-19 exhibit thrombotic coagulopathy](#)

"We report the clinical and laboratory coagulation characteristics of 27 pediatric and young adult patients (2 months to 21 years) treated for symptomatic COVID-19 at a children's hospital in the Bronx, New York, between March 1 and May 31, 2020. D-Dimer was > 0.5 µg/mL (upper limit of normal) in 25 (93%) patients at admission; 11 (41%) developed peak D-dimer > 5 µg/mL during admission. Seven (26%) patients developed venous thromboembolism: three with deep vein thrombosis and four with pulmonary embolism. Requirement of increased ventilatory support was a risk factor for thrombosis ($P = 0.006$). Three of eight (38%) patients on prophylactic anticoagulation developed thrombosis; however, no patients developed VTE on low-molecular-weight heparin prophylaxis titrated to anti-Xa level. Manifestation of COVID-19 disease was severe or critical in 16 (59%) patients. Four (15%) patients died of COVID-19 complications: all had comorbidities. Elevated D-dimer and increased VTE rate were observed in this young cohort, particularly in those with severe respiratory complications, suggesting thrombotic coagulopathy. More data are needed to guide thromboprophylaxis in this age group."

03 March 2021

Mil Med: [U.S. Neurosurgical Response to COVID-19: Forging a Path Toward Disaster Preparedness](#)

"The worldwide COVID-19 pandemic poses challenges to healthcare capacity and infrastructure. The authors discuss the structure and efficacy of the U.S. Navy's response to COVID-19 and evaluate the utility of this endeavor, with the objective of providing future recommendations for managing worldwide healthcare and medical operational demands from the perspective of Navy Neurosurgery.

The authors present an extensive review of topics and objectively highlight the efforts of U.S. Navy Neurosurgery as it pertains to the humanitarian mission during the COVID-19 pandemic.

During the humanitarian mission (March 27, 2020–April 14, 2020), the response of active duty and reserve neurosurgeons in the U.S. Navy was robust. Neurosurgical coverage was present on board the U.S. Navy Ships Mercy and Comfort, with additional neurosurgical deployment to New York City for intensive care unit management and coverage.

The U.S. Navy neurosurgical response to the COVID-19 pandemic was swift and altruistic. Although neurosurgical pathologies were limited among the presenting patients, readiness and manpower continue to be strong influences within the Armed Forces. The COVID-19 response demonstrates that neurosurgical assets can be rapidly mobilized and deployed in support of wartime, domestic, and global humanitarian crises to augment both trauma and critical care capabilities."

[PLoS Med: Early versus deferred anti-SARS-CoV-2 convalescent plasma in patients admitted for COVID-19: A randomized phase II clinical trial](#)

"The study was an open-label, single-center randomized clinical trial performed in an academic medical center in Santiago, Chile, from May 10, 2020, to July 18, 2020, with final follow-up until August 17, 2020. The trial included patients hospitalized within the first 7 days of COVID-19 symptom onset, presenting risk factors for illness progression and not on mechanical ventilation. The intervention consisted of immediate CP (early plasma group) versus no CP unless developing prespecified criteria of deterioration (deferred plasma group). Additional standard treatment was allowed in both arms. The primary outcome was a composite of mechanical ventilation, hospitalization for >14 days, or death. The key secondary outcomes included time to respiratory failure, days of mechanical ventilation, hospital length of stay, mortality at 30 days, and SARS-CoV-2 real-time PCR clearance rate. Of 58 randomized patients (mean age, 65.8 years; 50% male), 57 (98.3%) completed the trial. A total of 13 (43.3%) participants from the deferred group received plasma based on clinical aggravation. We failed to find benefit in the primary outcome (32.1% versus 33.3%, odds ratio [OR] 0.95, 95% CI 0.32–2.84, $p > 0.999$) in the early versus deferred CP group. The in-hospital mortality rate was 17.9% versus 6.7% (OR 3.04, 95% CI 0.54–17.17 $p = 0.246$), mechanical ventilation 17.9% versus 6.7% (OR 3.04, 95% CI 0.54–17.17, $p = 0.246$), and prolonged hospitalization 21.4% versus 30.0% (OR 0.64, 95% CI, 0.19–2.10, $p = 0.554$) in the early versus deferred CP group, respectively. The viral clearance rate on day 3 (26% versus 8%, $p = 0.204$) and day 7 (38% versus 19%, $p = 0.374$) did not differ between groups. Two patients experienced serious adverse events within 6 hours after plasma transfusion. The main limitation of this study is the lack of statistical power to detect a smaller but clinically relevant therapeutic effect of CP, as well as not having confirmed neutralizing antibodies in donor before plasma infusion.

In the present study, we failed to find evidence of benefit in mortality, length of hospitalization, or mechanical ventilation requirement by immediate addition of CP therapy in the early stages of COVID-19 compared to its use only in case of patient deterioration."

02 March 2021

Nat Med: [SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma](#)

"SARS-CoV-2 501Y.V2 (B.1.351), a novel lineage of coronavirus causing COVID-19, contains substitutions in two immunodominant domains of the spike protein. Here, we show that pseudovirus expressing 501Y.V2 spike protein completely escapes three classes of therapeutically relevant antibodies. This pseudovirus also exhibits substantial to complete escape from neutralization, but not binding, by convalescent plasma. These data highlight the prospect of reinfection with antigenically distinct variants and foreshadow reduced efficacy of spike-based vaccines."

ICYMI (older than the last 2 weeks)

J Med Internet Res: [Infection Control Behavior at Home During the COVID-19 Pandemic: Observational Study of a Web-Based Behavioral Intervention \(Germ Defence\)](#) (27 February 2021)

"Objective: This study aims to report current household infection control behaviors in the United Kingdom and examine how they might be improved.

Methods: This was a pragmatic cross-sectional observational study of anonymous participant data from Germ Defence between May 6-24, 2020. Germ Defence is an open-access fully automated website providing behavioral advice for infection control within households. A total of 28,285 users sought advice from four website pathways based on household status (advice to protect themselves generally, to protect others if the user was showing symptoms, to protect themselves if household members were showing symptoms, and to protect a household member who is at high risk). Users reported current infection control behaviors within the home and intentions to change these behaviors.

Results: Current behaviors varied across all infection control measures but were between sometimes (face covering: mean 1.61, SD 1.19; social distancing: mean 2.40, SD 1.22; isolating: mean 2.78, SD 1.29; putting packages and shopping aside: mean 2.75, SD 1.55) and quite often (cleaning and disinfecting: mean 3.17, SD 1.18), except for handwashing (very often: mean 4.00, SD 1.03). Behaviors were similar regardless of the website pathway used. After using Germ Defence, users recorded intentions to improve infection control

behavior across all website pathways and for all behaviors (overall average infection control score mean difference 0.30, 95% CI 0.29-0.31).

Conclusions: Self-reported infection control behaviors other than handwashing are lower than is optimal for infection prevention, although handwashing is much higher. Advice using behavior change techniques in Germ Defence led to intentions to improve these behaviors. Promoting Germ Defence within national and local public health and primary care guidance could reduce COVID-19 transmission."

J Gen Intern Med: [Mapping Inequality in SARS-CoV-2 Household Exposure and Transmission Risk in the USA](#)

"Health policy experts from Stanford University in California mapped inequalities in transmission and household COVID-19 exposure risk in the United States using a publicly available dataset (see summary). They found 5.6% of the population live in high-risk households (see summary for definition); most members of these households are people of color (76%) and live below 200% of the poverty line (58%)(Figure 1). Given these structural inequities in COVID-19 risk, authors suggest public health campaigns (testing, vaccination etc.) should focus on such households and policies facilitating prevention measures (i.e. paid time off, temporary housing for quarantine) must be implemented." (summary from [COVID19LST](#))

Clin Infect Dis: [Patients with uncomplicated COVID-19 have long-term persistent symptoms and functional impairment similar to patients with severe COVID-19: a cautionary tale during a global pandemic](#) (07 February 2021)

"To assess the prevalence of persistent functional impairment after COVID-19, we assessed 118 individuals 3-4 months after their initial COVID-19 diagnosis with a symptom survey, work productivity and activity index questionnaire, and 6-minute walk test. We found significant persistent symptoms and functional impairment, even in non-hospitalized patients with COVID-19."

J Clin Nurs: Best-Practices for Preventing Skin Injury Beneath Personal Protective Equipment During the COVID-19 Pandemic: A Position Paper from the National Pressure Injury Advisory Panel (NPIAP) (03 February 2021)

"COVID-19 has infected millions of patients and impacted healthcare workers worldwide. Personal Protective Equipment (PPE) is a key component of protecting frontline clinicians against infection. The benefits of PPE far outweigh the risks, nonetheless, many clinicians are exhibiting skin injury caused by PPE worn incorrectly. These skin injuries, ranging from lesions to open wounds are concerning because they increase the susceptibility of viral infection and transmission to other individuals. Early into the COVID-19 pandemic (April 2020), the U.S. National Pressure Injury Advisory Panel (NPIAP) developed a series of

position statements to improve wear-ability of PPE and protect healthcare professionals and their patients as safe from harm as possible under the circumstances. The NPIAP positions, which were formed by conducting a systematic review of what was known at the time, include: (1) Prepare skin before and after wearing PPE with skin sealants, barrier creams and moisturizers; (2) Frequent PPE offloading to relieve pressure and shear applied to skin; (3) treat visible skin injuries immediately caused by PPE to minimize future infection; (4) non-porous dressings may provide additional skin protection, but lack evidence; (5) health systems should take care to educate clinicians about placement and personal hygiene related to handling PPE. Throughout all of these practices, handwashing remains a top priority to handle PPE. These NPIAP positions provided early guidance to reduce the risk of skin injury caused by PPE based on available research regarding PPE injuries, a cautious application of evidence-based recommendations on prevention of device related pressure injuries in patients and the expert opinion of the NPIAP Board of Directors. Clinicians who adhere to these recommendations reduce the prospects of skin damage and long-term effects (e.g. scarring). These simple steps to minimize the risk of skin injury and reduce the risk of coronavirus infection from PPE can help."

Emerg Infect Dis: [Prevalence of SARS-CoV-2 Antibodies in First Responders and Public Safety Personnel, New York City, New York, USA, May–July 2020](#) (published online 25 January 2021)

"We conducted a serologic survey in public service agencies in New York City, New York, USA, during May–July 2020 to determine prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among first responders. Of 22,647 participants, 22.5% tested positive for SARS-CoV-2-specific antibodies. Seroprevalence for police and firefighters was similar to overall seroprevalence; seroprevalence was highest in correctional staff (39.2%) and emergency medical technicians (38.3%) and lowest in laboratory technicians (10.1%) and medicolegal death investigators (10.8%). Adjusted analyses demonstrated association between seropositivity and exposure to SARS-CoV-2-positive household members (adjusted odds ratio [aOR] 3.52 [95% CI 3.19–3.87]), non-Hispanic Black race or ethnicity (aOR 1.50 [95% CI 1.33–1.68]), and severe obesity (aOR 1.31 [95% CI 1.05–1.65]). Consistent glove use (aOR 1.19 [95% CI 1.06–1.33]) increased likelihood of seropositivity; use of other personal protective equipment had no association. Infection control measures, including vaccination, should be prioritized for frontline workers."

Selected Literature: Preprints

Preprints are found on preprint servers such as [arXiv](#), [bioRxiv](#), and [medRxiv](#); they are commonly used for biomedical research. Preprints may later be published in peer-reviewed journals. Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review.

They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

medRxiv: [Tocilizumab efficacy in COVID-19 patients is associated with respiratory severity-based stages](#) (09 March 2021)

"Background: Tocilizumab treatment is investigated, and effectiveness in ICU-admitted COVID-19 patients has been reported. Although controversy exists regarding the efficacy of tocilizumab treatment, it has been suggested that tocilizumab might show positive results depending on patient severity status. We examined an association between tocilizumab and distinct disease severity stages.

Methods and Findings: From March 3 to March 23 2020, 494 consecutively admitted COVID-19 patients received tocilizumab or standard treatment alone. Data were obtained retrospectively. Clinical respiratory severity (CRS) stages were defined by patient oxygenation status and were also associated to scores of WHO clinical progression scale. We categorized patients in three stages, mild/moderate CRS1 ($\text{FiSpO}_2 < 0.35$; WHO score 5), moderate/severe CRS2 ($\text{FiO}_2 = 0.5/\text{high flow mask}$; WHO score 6) and severe/critical CRS3 ($\text{FiO}_2 < 80\%/\text{high flow/prone position or mechanical ventilation}$; score > 6). The primary outcome was the composite of death or ICU admission in patients of stages CRS1, CRS2, and CRS3, as well as in total patients. We also addressed mortality alone in total patients. Kaplan-Maier curves, Cox proportional regression and inverse probability weighting marginal structural models were used. We conducted the study from March 3 to April 7 2020 with broad-ranged severity patients; 167 tocilizumab-treated and 327 untreated. CRS1 patients showed no apparent benefit after treatment, while the risk of the primary outcome was greatly reduced in CRS2 treated participants ((HR=0.22; 95% CI (0.16-0.44)). Moreover, tocilizumab treatment was associated with significantly decreased CRS2 patient proportion that reached the outcome compared to non-treated controls (27.8.0% vs. 65.4%; $p < 0.001$). Severe/critical CRS3 patients, also showed benefit after treatment (HR=0.38; 95% CI (0.16-90)), although not as robust as was that of CRS2 treated individuals. Tocilizumab was associated with reduced outcome risk in total patients (HR=0.42; 95% CI (0.26-0.66)) after CRS adjustment, but not if CRS classification was not accounted as confounding factor (HR=1.19; 95% CI (0.84-1.69)). The outcome of mortality alone upon tocilizumab treatment was significant (HR=0.58; 95% CI (0.35-0.96)) after accounting for CRS classification.

Conclusions: Tocilizumab treatment is associated with reduced COVID-19 escalation in CRS2 patients, suggesting efficacy in moderate/severe non-ICU-admitted patients. CRS classification could represent an essential confounding factor in evaluating tocilizumab in studies of broad-ranged severity patients."

medRxiv: [COVID-19 vaccine response in pregnant and lactating women: a cohort study](#) (08 March 2021)

"Background: Pregnant and lactating women were excluded from initial COVID-19 vaccine trials; thus, data to guide vaccine decision-making are lacking. We sought to evaluate the immunogenicity and reactogenicity of COVID-19 mRNA vaccination in pregnant and lactating women.

Methods: 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant) were enrolled in a prospective cohort study at two academic medical centers. Titers of SARS-CoV-2 Spike and RBD IgG, IgA and IgM were quantified in participant sera (N=131), umbilical cord sera (N=10), and breastmilk (N=31) at baseline, 2nd vaccine dose, 2-6 weeks post 2nd vaccine, and delivery by Luminex, and confirmed by ELISA. Titers were compared to pregnant women 4-12 weeks from native infection (N=37). Post-vaccination symptoms were assessed. Kruskal-Wallis tests and a mixed effects model, with correction for multiple comparisons, were used to assess differences between groups.

Results: Vaccine-induced immune responses were equivalent in pregnant and lactating vs non-pregnant women. All titers were higher than those induced by SARS-CoV-2 infection during pregnancy. Vaccine-generated antibodies were present in all umbilical cord blood and breastmilk samples. SARS-CoV-2 specific IgG, but not IgA, increased in maternal blood and breastmilk with vaccine boost. No differences were noted in reactogenicity across the groups.

Conclusions: COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in non-pregnant women. Vaccine-induced immune responses were significantly greater than the response to natural infection. Immune transfer to neonates occurred via placental and breastmilk."

medRxiv: [Persistence of symptoms up to 10 months following acute COVID-19 illness](#) (08 March 2021)

"Importance: COVID-19 symptoms are increasingly recognized to persist among a subset of individual following acute infection, but features associated with this persistence are not well-understood. Objective: We aimed to identify individual features that predicted persistence of symptoms over at least 2 months at the time of survey completion. Design: Non-probability internet survey.

Participants were asked to identify features of acute illness as well as persistence of symptoms at time of study completion. We used logistic regression models to examine association between sociodemographic and clinical features and persistence of symptoms at or beyond 2 months. Setting: Ten waves of a fifty-state survey between June 13, 2020

and January 13, 2021. Participants: 6,211 individuals who reported symptomatic COVID-19 illness confirmed by positive test or clinician diagnosis. Exposure: symptomatic COVID-19 illness

Results: Among 6,211 survey respondents reporting COVID-19 illness, with a mean age of 37.8 (SD 12.2) years and 45.1% female, 73.9% white, 10.0% Black, 9.9% Hispanic, and 3.1% Asian, a total of 4946 (79.6%) had recovered within less than 2 months, while 491 (7.9%) experienced symptoms for 2 months or more. Of the full cohort, 3.4% were symptomatic for 4 months or more and 2.2% for 6 months or more. In univariate analyses, individuals with persistent symptoms on average reported greater initial severity. In logistic regression models, older age was associated with greater risk of persistence (OR 1.10, 95% CI 1.01-1.19 for each decade beyond 40); otherwise, no significant associations with persistence were identified for gender, race/ethnicity, or income. Presence of headache was significantly associated with greater likelihood of persistence (OR 1.44, 95% CI 1.11-1.86), while fever was associated with diminished likelihood of persistence (OR 0.66, 95% CI 0.53-0.83).

Conclusion and Relevance: A subset of individuals experience persistent symptoms from 2 to more than 10 months after acute COVID-19 illness, particularly those who recall headache and absence of fever. In light of this prevalence, strategies for predicting and managing such sequelae are needed."

bioRxiv: [Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees](#) (posted 01 March 2021)

"The emergence of SARS-CoV-2 variants highlighted the need to better understand adaptive immune responses to this virus. It is important to address whether also CD4+ and CD8+ T cell responses are affected, because of the role they play in disease resolution and modulation of COVID-19 disease severity. Here we performed a comprehensive analysis of SARS-CoV-2-specific CD4+ and CD8+ T cell responses from COVID-19 convalescent subjects recognizing the ancestral strain, compared to variant lineages B.1.1.7, B.1.351, P.1, and CAL.20C as well as recipients of the Moderna (mRNA-1273) or Pfizer/BioNTech (BNT162b2) COVID-19 vaccines. Similarly, we demonstrate that the sequences of the vast majority of SARS-CoV-2 T cell epitopes are not affected by the mutations found in the variants analyzed. Overall, the results demonstrate that CD4+ and CD8+ T cell responses in convalescent COVID-19 subjects or COVID-19 mRNA vaccinees are not substantially affected by mutations found in the SARS-CoV-2 variants."

medRxiv: [Household COVID-19 risk and in-person schooling](#) (posted 01 March 2021)

"In-person schooling has proved contentious and difficult to study throughout the SARS-CoV-2 pandemic. Data from a massive online survey in the United States indicates an increased risk of COVID-19-related outcomes among respondents living with a child attending school in-person. School-based mitigation measures are associated with

significant reductions in risk, particularly daily symptoms screens, teacher masking, and closure of extra-curricular activities. With seven or more mitigation measures, the association between in-person schooling and COVID-19-related outcomes all but disappears. Teachers working outside the home were more likely to report COVID-19-related outcomes, but this association is similar to other occupations (e.g., healthcare, office work). In-person schooling is associated with household COVID-19 risk, but this risk can likely be controlled with properly implemented school-based mitigation measures."

News in Brief

CDC Director: "There is so much that's critical riding on the next two months... How quickly we will vaccinate versus whether we will have another surge really relies on what happens in March and April" ([CNN](#)).

The New Variants

A variant in Oregon looks like the UK variant (B.1.1.7) but with a mutation that may make it less susceptible to vaccines ([NYT](#)).

"Multitude of coronavirus variants found in the US — but the threat is unclear" ([Nature](#)).

Long read: "A massive global hunt for variants is under way: Tracking the coronavirus's evolution, letter by letter, has given us a powerful tool—if we can figure out how to use it" ([Atlantic](#)).

Vaccines

"Pfizer/BioNTech say data suggests vaccine 94% effective in preventing asymptomatic infection" ([Reuters](#)).

1 in 4 Americans are not willing to get a COVID-19 vaccine ([MU](#)).

"In Palm Beach, Covid-19 vaccines intended for rural Black communities are instead going to wealthy white Floridians" ([STAT](#)).

"The differences between the vaccines matter: Yes, all of the COVID-19 vaccines are very good. No, they're not all the same" ([Atlantic](#)).

Testing

The first molecular, nonprescription, at-home test for COVID-19 has received EUA; cost and availability is unclear at the time of this writing ([FDA](#)).

Almost half of testing labs in the US have trouble getting supplies to meet demand ([BusinessWire](#)).

Treatments

"We have vaccines for COVID-19. Why don't we have good treatments?" ([BuzzFeed](#))

Although it was shown to be a safe treatment, no benefit was seen with convalescent plasma in emergency department patients with mild symptoms of COVID-19 ([NIH](#)).

The RECOVERY trial has stopped recruitment for its colchicine study after a data monitoring board saw 'no convincing evidence' of benefit ([Endpoints](#)).

"Study shows more than half of hospitalized COVID-19 patients in U.S. received antibiotics in pandemic's first six months" ([Pew](#)).

Leronlimab, an anti-CCR5 antibody, has failed Phase IIb/III trial for COVID-19 ([Endpoints](#)).

Adding tocilizumab to remdesivir failed to shorten time to discharge in patients hospitalized with severe COVID-19 pneumonia ([Genentech](#)).

The FDA has detailed why you shouldn't use ivermectin to treat or prevent COVID-19 ([FDA](#)).

On a more positive note, a Phase 3 trial (BLAZE-1) of bamlanivimab and etesevimab together reduced hospitalizations and death in high risk COVID-19 patients ([Lilly](#)).

Data

The HHS inspector general is looking at how the CDC "can improve the accuracy of its data" regarding race and ethnicity ([Politico](#)).

"Pregnancy and COVID: what the data say – pregnant women fare worse than others, although the risks to the fetus are slight" ([Nature](#)).

Long COVID

The NIH is investing \$1 billion to investigate long COVID, including tracking patient recovery and hosting a biospecimen bank ([Nature](#)).

"Children's hospitals grapple with young Covid 'long haulers'" ([KHN](#)).

Long read: "Unlocking the mysteries of long COVID " ([Atlantic](#)).

Thanks, Coronavirus

"When more Covid-19 data doesn't equal more understanding" ([MIT News](#)).

The American Board of Internal Medicine has extended its MOC requirements until the end of 2022 ([ABIM](#)).

And Now for Something Completely Different

Check out the winners of the 2020 world nature photography awards ([WNPA](#)).

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Statistics

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VA DOH: Virginia Department of Health. COVID-19 in Virginia. Link: <http://www.vdh.virginia.gov/coronavirus/>

One Year Later

BuzzFeed: BuzzFeed News. Tom Hanks, The NBA, And COVID's Day Of Reckoning In The US: An Oral History (11 March 2021). Link:

<https://www.buzzfeednews.com/article/buzzfeednews/march-11-covid-tom-hanks-nba-who>

NPR: National Public Radio. Laurel Wamsley. March 11, 2020: The Day Everything Changed (11 March 2021). Link: <https://www.npr.org/2021/03/11/975663437/march-11-2020-the-day-everything-changed>

SciAm: Scientific American. Tanya Lewis. How the U.S. Pandemic Response Went Wrong—and What Went Right—during a Year of COVID (11 March 2021). Link:

<https://www.scientificamerican.com/article/how-the-u-s-pandemic-response-went-wrong-and-what-went-right-during-a-year-of-covid/>

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Tracy C. Shields, MSIS, AHIP (Reference Medical Librarian at NMCP, Library Services)

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